REMARKS

Claims 1-35 are pending. Claims 1, 4, 11, and 30 have been amended. Claims 3, 5, 6, 8, 10, 12-16, 20-26, and 28-35 have been withdrawn.

Restriction

Applicants have found the list of withdrawn claims provided by the examiner to be confusing, and have amended that list in a manner that they believe conforms with the elected group and species as follows:

- Claims 4 and 11 were the originally elected claims in Group II, and comply with the species requirements. Therefore, they should be included in the claims to be examined, and should not be withdrawn.
- Applicants elected ε-amino caproic acid, an amino acid that is not gene coded, as one of the species. Therefore, claim 9, rather than claim 8, should be examined, and claim 8, not claim 9, should be withdrawn.
- Claim 27 is listed as being both withdrawn and rejected. Claim 27 depends from claim 19, and should be examined, not withdrawn.

If applicants are wrong in their indication of which claims should and should not be withdrawn, they request that the examiner clarify the restriction.

Rejection of Claims 1, 2, 7, and 8 under 35 USC § 102(b)

The examiner has rejected claims 1, 2, 7, and 8 (which, under applicants' understanding of the restriction, should be claims 1, 2, 4, 7, 9 and 11) as being anticipated by Lorenzen, et al., The Journal of Cell Biology (1995) 131:631-643 ("Lorenzen"). Applicants traverse this rejection.

First, claims 1, 4, and 11 have been amended to increase the minimum length of the arginine-containing region from 5 subunits to 7 subunits. Assuming Y in claims 1, 4 and 11 is a lysine (K), the shortest arginine-containing region would be RKRKRKR. This is not the same as the RKRKR region found in Lorenzen. Therefore Lorenzen does not anticipate this element.

Second, the transport compound studied in Lorenzen is 100 amino acids long (β-galTC316-415) or 72 amino acids long (β-galactosidase fusion protein carrying the terminal 72 residues of the $p45^{TC}$). The compounds of the present claims have transporters composed of at most 21 amino acid residues for $(ZY_m)Z$, up to 41 amino acid residues for $(ZYYY)_nZ$. There is no identity, or similarity between Lorenzen and the present claims on this element.

Third, the compounds studied in Lorenzen were synthesized inside the cells where localization was studied. No evidence was provided that these compounds could act as transporters to bring a therapeutic or diagnostic agent into a cell through the cell membrane. In fact, Lorenzen states "[t]he data presented here demonstrate that the 48-kD and 45-kD forms of TCPTP localize to the ER and nucleus, respectively." page 639, *Discussion*, paragraph 1. Thus, the Lorenzen compounds are not even being tested for the same purpose as those of the present invention.

Because of all of these differences between Lorenzen and the present claims, applicants request that the examiner withdraw the novelty rejection.

Rejection of Claims 1, 2, 7, 8, 17-19 and 27 Under 35 USC § 103(a)

The examiner has rejected claims 1, 2, 7, 8, 17-19, and 27 as obvious over Lorenzen in view of US Patent No. 4,409,141 to Noda et al., ("Noda"). As these are all of the claims listed in the office action as being currently prosecuted, applicants believe that the examiner would also include claims 4, 9, and 11, and not claim 8, were he to follow the determination of claims that meet the restriction requirement as described above. Therefore, applicants are responding to this rejection as though it is to claims 1, 2, 4, 7, 9, 17-19 and 27.

Applicants traverse this rejection. As described above, Lorenzen does not teach the same invention as is claimed by the applicants. Among other points, Lorenzen does not teach targeting a molecule from outside the cell through the cellular membrane, into the cell. Instead, Lorenzen teaches production of a protein, including several chimeras, inside the cell, and determining where in the same cell the protein localizes, if at all. On the other hand, the present invention provides compositions and methods for enhancing transport of biological agents from outside a cell into the cell.

The composition of the Lorenzen compounds is significantly different from those of the present invention. The Lorenzen compounds are proteins, in some cases chimeric, shortened,

and/or internally mutated. They are made by genetically modifying a plasmid into which a selected gene has been engineered (the TCPTP gene). See Lorenzen page 632, "Construction of Expression Vectors." In order to allow the plasmid to replicate to provide protein for Lorenzen's experiments, only amino acids can be added to the plasmid. Even then, the only amino acids that can be added are those that do not interfere with the replication of the plasmid or the transcription and translation of the gene into the desired protein. It would not be logical to introduce a linker having a chemical structure different from that of an amino acid or peptide, as insufficient (if any) protein to be studied would be produced inside the cell.

Contrary to what the examiner has stated on page 5 of the March 15, 2006 office action, Lorenzen does not teach the need for a spacer between two elements of the transporter sequence. At page 639, column 2, second paragraph, Lorenzen shows that there is no upstream element that is required with the RKRKR downstream element. Neither point mutations nor deletions in the putative upstream element and/or in the spacer between that putative upstream and downstream elements had any effect on the transportation capabilities of the compound. Thus there is no spacer or need for a linker in Lorenzen. There is no teaching or suggestion to combine Lorenzen and Noda.

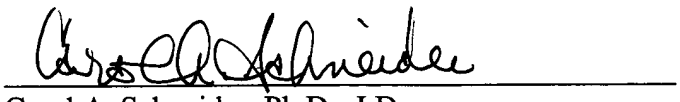
In contrast, the present claims cover a peptide transporter region, a non peptide linker, and a biologically active compound that can, but need not be, a protein. A linker is needed to join the transporter region to the biological agent. The conformation of the compound must be retained in order to achieve transportation of the biologically active compound into a cell.

Even if there were some reason to add a linker/spacer to Lorenzen, Noda's spacer does not meet the requirements of the linker of the present invention. In order to join the transporter region with the biologically active compound in a manner that does not interfere with the function of the transporter, only linkers with certain conformations can be used. Four families of useful linkers are provided by, and claimed in, the present application. They have no overall structural similarity to the Noda linker (S-acetylmercapto succinic anhydride). There would be no reason to believe that such a linker would work in the present invention, even based on hindsight, an analysis that is not allowed under patent law. *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566 (Fed. Cir. 1996).

CONCLUSION

Based on the discussion above, the current claims are neither anticipated by Lorenzen nor made obvious by the combination of Lorenzen and Noda. Applicants therefore request that the examiner withdraw these rejections and issue a Notice of Allowance. If the examiner believes that contacting the undersigned would be helpful in the prosecution of this case, he is invited to contact her at (650) 251-7702 or caschneider@mintz.com.

Respectfully submitted,

By: 

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